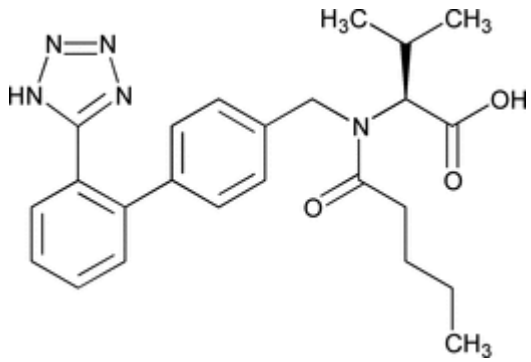
Valsartan



$C_{24}H_{29}N_5O_3$ 435.52

L-Valine, *N*-(1-oxopentyl)-*N*-[[2′-(1*H*-tetrazol-5-yl)[1,1′-biphenyl]-4-yl]methyl]-;
N-[*p*-(*o*-1*H*-Tetrazol-5-ylphenyl)benzyl]-*N*-valeryl-L-valine [137862-53-4].

DEFINITION

Valsartan contains NLT 98.0% and NMT 102.0% of valsartan ($C_{24}H_{29}N_5O_3$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

- **A. ▲Spectroscopic Identification Tests** ⟨197⟩**,** *Infrared Spectroscopy*: **197M**▲ (CN 1-May-2020)
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **Procedure**

Mobile phase: Acetonitrile, glacial acetic acid, and water (500:1:500)
Standard solution: 0.5 mg/mL of USP Valsartan RS in *Mobile phase*
Sample solution: 0.5 mg/mL of Valsartan in *Mobile phase*
Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 273 nm
Column: 3.0-mm × 12.5-cm; 5-µm packing L1
Flow rate: 0.4 mL/min
Injection volume: 10 µL
System suitability
Sample: *Standard solution*
Suitability requirements
Relative standard deviation: NMT 2.0%
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of valsartan ($C_{24}H_{29}N_5O_3$) in the portion of Valsartan taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of the *Sample solution*
r_S = peak response of the *Standard solution*
C_S = concentration of USP Valsartan RS in the *Standard solution* (mg/mL)
C_U = concentration of Valsartan in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

- **Residue on Ignition** ⟨281⟩**:** NMT 0.1%
- **Procedure 1: Limit of Valsartan Related Compound A**

Mobile phase: *n*-Hexane, 2-propanol, and trifluoroacetic acid (850:150:1)
System suitability solution: 0.04 mg/mL each of USP Valsartan Related Compound A RS and USP Valsartan RS in *Mobile phase*
Standard solution: 0.01 mg/mL of USP Valsartan Related Compound A RS in *Mobile phase*
Sample solution: 1 mg/mL of Valsartan in *Mobile phase*. Sonicate for 5 min.
Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 230 nm
Column: 4.6-mm × 25-cm; 5-µm packing L40
Flow rate: 0.8 mL/min
Injection volume: 10 µL
System suitabili
Sample: *System s ability solution*
Suitability requirem nts
Resoluti n: T 2.0 etween valsartan related comp und A d valsartan
Relative st nda d deviation: NMT 5% for valsartan re ed co und A peak
Analysis
Samples *tandard solution* and *Sample solution*
Calcul te the percentage of valsartan related compound A in t portion of Valsartan taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of valsartan related compound A from the *Sample solution*
r_S = peak response of valsartan related compound A from the *Standard solution*
C_S = concentration of USP Valsartan Related Compound A RS in the *Standard solution* (mg/mL)
C_U = concentration of Valsartan in the *Sample solution* (mg/mL)

Acceptance criteria: NMT 1.0% of valsartan related compound A.

- **Procedure 2: Limit of Valsartan Related Compound B, Valsartan Related Compound C, and Other Related Compounds**

Mobile phase: Proceed as directed in the *Assay*.
Standard solution: 1 µg/mL each of USP Valsartan RS, USP Valsartan Related Compound B RS, and USP Valsartan Related Compound C RS in *Mobile phase*
Sample solution: 0.5 mg/mL of Valsartan in *Mobile phase*
Chromatographic system: Proceed as directed in the *Assay*, except for the following.
Detector: UV 225 nm
System suitability
Sample: *Standard solution*
Suitability requirements
Resolution: NLT 1.8 between valsartan related compound B and valsartan
Relative standard deviation: NMT 10.0% for valsartan related compound B and NMT 2.0% for valsartan
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the percentage of valsartan related compound B and valsartan related compound C in the portion of Valsartan taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of valsartan related compound B or valsartan related compound C from the *Sample solution*
r_S = peak response of valsartan related compound B or valsartan related compound C from the *Standard solution*
C_S = concentration of USP Valsartan Related Compound B RS or USP Valsartan Related Compound C RS in the *Standard solution* (mg/mL)
C_U = concentration of Valsartan in the *Sample solution* (mg/mL)

Calculate the percentage of any other impurity in the portion of Valsartan taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response of any other impurity from the *Sample solution*
r_S = peak response of valsartan from the *Standard solution*
C_S = concentration of USP Valsartan RS in the *Standard solution* (mg/mL)
C_U = concentration of Valsartan in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 1*.

Table 1

Name	Acce ce Cri er MT (%)
Valsartan related compound B[a]	2
Valsartan related compound C[b]	0.
Any other individual impurity[c]	0.1

Table 1 *(continued)*

Name	Acceptance Criteria, NMT (%)
Total impurities[c]	0.3

[a] *N*-Butyryl-*N*-{[2′-(1*H*-tetrazole-5-yl)biphenyl-4-yl]methyl}-L-valine.
[b] *N*-Valeryl-*N*-{[2′-(1*H*-tetrazole-5-yl)biphenyl-4-yl]methyl}-L-valine benzyl ester.
[c] Excluding valsartan related compound A.

SPECIFIC TESTS

- **WATER DETERMINATION,** *Method I* ⟨921⟩**:** NMT 2.0%
- **ABSORBANCE**
  Analytical wavelength: 420 nm
  Sample solution: A 1-in-20 solution of valsartan in methanol
  Acceptance criteria: The absorbance divided by the path length is NMT 0.02.

ADDITIONAL REQ IREMENTS

- **PACKAGING AND ST AGE:** Preserve in tight containers, and store at con led ro temperature. Protect from moisture nd h
- **U REFE ENCE S DARDS** ⟨11⟩
  USP Valsarta RS
  USP artan lated Compound A RS
  N Vale l *N*-{[2′-(1*H*-tetrazole-5-yl)biphenyl-4-yl] methyl} D-valine.
  $C_{24}H$ N_5O_3 435.52
  USP Valsartan Related Compound B RS
  Butyryl-*N*-{[2′-(1*H*-tetrazole-5-yl)biphenyl-4-yl] methyl}-L-valine.
  $C_{23}H_{27}N_5O_3$ 421.49
  USP Valsartan Related Compound C RS
  N-Valeryl-*N*-{[2′-(1*H*-tetrazole-5-yl)biphenyl-4-yl] methyl}-L-valine benzyl ester.
  $C_{31}H_{35}N_5O_3$ 525.64